Medical Lib.

MAR 13 1928

Volume X MARCH, 1928 Number 3

THE JOURNAL OF INDUSTRIAL HYGIENE

AND ABSTRACT OF THE LITERATURE

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Chronic Benzol Poisoning among Women Industrial Workers: A Study of the Women Exposed to Benzol Fumes in Six Factories

The Physiology of Industrial Hygiene: II. The Physiologic Effects of Exercise and Mental Effort on the Circulation, and their Relation to Industry

Published at Mount Royal and Guilford Aves., Baltimore, Md.
by HARVARD SCHOOL OF PUBLIC HEALTH

Entered as second-class matter, at the Post Office at Baltimore, Maryland, under Act of March 3, 1879.
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THE JOURNAL OF INDUSTRIAL HYGIENE

VOLUME X | MARCH, 1928 | NUMBER 3

CHRONIC BENZOL POISONING AMONG WOMEN INDUSTRIAL WORKERS: A STUDY OF THE WOMEN EXPOSED TO BENZOL FUMES IN SIX FACTORIES*

ADELAIDE ROSS SMITH, M.D.

INTRODUCTION

LARGELY as a result of the striking Final Report of the Committee on Benzol of the National Safety Council regarding the hazards of benzol in industry, published in May, 1926, and because it was felt that more information is needed regarding the early effect of benzol upon women, the Bureau of Women in Industry of the New York State Department of Labor decided to make a study of women workers exposed to benzol in New York State. The object of this study was to secure data with regard to the prevalence of unrecognized chronic benzol poisoning among women at work and also with regard to its earliest signs and symptoms among them. Six factories, distributed among the large industrial centers of the state, were found where conditions lent themselves to this study. One manufactured tires and rubber goods; one, cameras; one, shoes; and three, sanitary tin cans. The study was made in the summer and fall of 1926.

Examinations were made, with but few exceptions, of all the women who were exposed to benzol in each plant. A history of each was taken covering age, occupation, mode of exposure to benzol, length of exposure, past medical history with special reference to menstrual irregularities and miscarriages or stillbirths, and complaints which had arisen since exposure. The weight and the blood pressure were taken whenever possible; notes were made on the appearance of the individual and in every case a complete

*Abstracted from Special Bulletin No. 150, Chronic Benzol Poisoning among Women Industrial Workers, from the Bureau of Women in Industry, New York State Department of Labor, February, 1927. Received for publication Dec. 19, 1927.

blood count was made. This included an estimation of the percentage of hemoglobin by the Newcomer method, and an estimation of the number of red and white blood cells, as well as a differential white blood cell count.

The workrooms where benzol was used were visited and the operations involving its use observed. It was not possible with the equipment at hand to make determinations of the concentration of benzol vapor in these rooms, therefore judgment as to the degree of contamination of the air could only be based empirically on the strength of the benzol odor. Statements as to the composition of the various compounds, cements, and lacquers mentioned are based on information obtained from factory officials. In no cases were samples analyzed.

The criteria upon which a presumptive diagnosis of benzol poisoning was based were the same as those employed by the Benzol Committee of the National Safety Council, namely, a history of exposure and a reduction of 25 per cent. or more in the white cell count (bringing it down to 5,625 or below, from the normal 7,500). This standard is a conservative one and is perhaps too arbitrary in that it attempts to set a sharp dividing line between positive and negative cases. It was, however, applied with a certain flexibility and those cases in which there was reason to believe that the benzol effect was present, even without an exact 25 per cent. reduction in the white count, were recorded as suspected cases of chronic poisoning. When there was a diminution in the white cell count amounting to 25 per cent. or more, on the other hand, cases were considered presumptively positive even though confirmatory evidence in the way of symptoms or other blood changes was, in some instances, lacking.

Description of Working Conditions

Factory 1 was a tire and rubber goods plant housed in a modern building with large, airy workrooms and having very good facilities for the comfort and convenience of the employees, including a cafeteria. A full time graduate nurse was employed and the plant was visited regularly by a physician. Benzol was used freely throughout the factory and about ten women were employed at operations which involved contact with it. It was used in two forms, as a clear liquid and as the solvent in a rubber cement. A brief description of the processes involving its use by women follows.

In the operation known as making "bends" to be used in tire building, the girls stood at tables upon which lengths of rubberized canvas were spread; dipping a cotton swab on a stick in an open pan of benzol standing on a table beside them, they applied it to the material which they then shaped on a drum and hung on a rack near at hand to dry. The women on this job used 6 to 7 quarts of benzol daily. Men worked at tire building in another part of the same room and it was said that in the busy season 50 gallons of benzol were consumed there daily. The workroom had very good general ventilation with windows on three sides, but no special ventilating devices to carry off the benzol fumes were provided.

There were several jobs requiring

the use of a benzol-rubber cement compounded of 1 pound of rubber to 1 gallon of benzol. One of these jobs was cementing the ends of short hose lengths. Here the worker stood before an open pan of cement into which she dipped the ends of the hose, which were then dried in the same room. As a rule she did 500 of these daily. Another girl standing not far behind her attached metal caps to the hose. In the same department benzol-rubber cement was used for applying rubber labels to hose and benzol was used freely for cleaning. In another department a woman standing before a long table applied the cement from an open bowl with her fingers to one edge of long strips of rubber to be made into hose. In all of these cases the general ventilation was good but no provision was made for local exhaust.

Of the ten women examined in this plant all but two had some complaints associated with their work. By this is meant either that symptoms which had not previously been present had developed after exposure to benzol, or that previously existing symptoms had become more frequent or more pronounced. These complaints were chiefly headache, dizziness, excessive fatigue, and nausea or loss of appetite. Two positive cases of poisoning and one suspected case were found.

The attitude on the part of the management toward the benzol hazard in this plant was distinctly casual and the medical department had no particular interest in it. No one seemed to be aware of the need for any precautions in its use except such as concerned the fire hazard. The only device for local ventilation to remove benzol fumes seen in the factory was a hood with an up draft over one trough of cement.

Factory 2 was a camera manufacturing plant with, again, very good general facilities. In differed from Factory 1 in that its well-equipped medical department was aware of the danger from benzol and had been attempting to keep track of the health of the benzol workers through semi-annual blood counts. The press of other work, however, had made it impossible to do this systematically.

In this plant women came in contact with benzol in two ways, through working with a benzol-rubber cement and through applying with a spray gun a lacquer containing benzol. The cement, composed of 90 per cent. by volume of benzol, was used for gluing together parts of the camera bellows. It was applied to the bellows with a paintbrush dipped in a practically open can standing on the workbench in front of each worker. When cemented, the bellows were placed on racks at the worker's side to await their second cementing. The room where this work was done was rather long and narrow. Although there were windows on two and a half sides, the natural ventilation was not particularly good owing to the fact that when the windows were widely opened there was a tendency to too much draft. The edges of the cementing benches had been equipped with a device designed to draw off the fumes by suction but the suction was too weak to have any appreciable effect and the odor of benzol in the room was decidedly noticeable. About fifty-five persons, men and women, worked in this room and 15 gallons of cement were used there daily. Thirty-three

women from this department were examined; nine of them worked with the cement; the remainder did not use it. Among this group of thirty-three, complaints of headache, dizziness, nervousness, weakness, and marked fatigue were extraordinarly common. Only six made no complaint. Eleven positive cases were found and one more was put on the suspected list.

In the same factory eight women were interviewed who did spray lacquering with a lacquer containing 4 per cent. by volume of benzol. The work was done under hoods but in most cases, owing to faulty construction and ventilation, the sprayed lacquer could be seen blowing out about the workers' faces. Five of the eight showed decreased white blood cell counts. Whether this exceedingly high proportion represents the degree of risk ordinarily associated with this type of work, it is impossible to say, since no more women lacquerers were examined, but there seems no reason for supposing that it may not be typical where ventilating hoods are inadequate.

The history of a woman in whom benzol poisoning had been suspected and who had been sent to the hospital for treatment was obtained from the plant physician. Though not diagnosed in the hospital as a case of benzol poisoning, it was included among the positive cases because it showed typical signs and symptoms of this condition. A résumé of the hospital record of this case is given below.

Case 4.—Age 28. Chief complaints: Weakness, shortness of breath, purpuric spots. Past history: No serious illnesses, always robust and vigorous until present illness. Employed since 1923 in the bellows department.

Present illness: Four months before admission to hospital she was found to be anemic by routine factory examination. She had no subjective symptoms and continued work. One month later she developed the first purpuric spot. It appeared on the shoulder and was about 6 cm. in diameter. The following week another spot appeared on the calf of the left leg. Nine weeks before admission she became acutely ill with an upper respiratory infection. She never fully regained strength and remained weak and short of breath. She reported for work but was unable to carry it on. Three weeks before admission a purpuric spot, the size of a silver dollar, appeared on the left thigh and another a few days later on the dorsum of the right hand. She was picked up again as a case of anemia by the factory medical department and sent to the hospital for study. She had had no spontaneous hemorrhages and menstrual flow was normal.

Family history: One brother had a period of purpura.

Physical examination on admission: Nutrition good; pale; slight thyroid enlargement; blood pressure 105/50; in the right axilla a mass of suppurating lymph nodes was found; on the lateral aspect of the left thigh there was a fading purpuric spot about $3\frac{1}{2}$ cm. in diameter; a fresh purpuric spot was found on the dorsum of the right hand. Wassermann negative; urine negative. The blood count was as follows:

Hemoglobin	70%
Red blood cells	3,020,000
White blood cells	3,600
Polymorphonuclears	57%
Lymphocytes	15%
Monocytes	27%
Eosinophils	1%

No pathologic white cells. Red cells show anisocytosis but no poikilocytosis. Platelets rare. Platelet count 25,000 per c.mm. Cell volume 30%. Bleeding time $2\frac{1}{4}$ minutes. Clot retraction time—none at 24 hours.

Course in hospital: The patient was put on a diet to combat anemia. The blood count, which was closely followed, showed

steady loss in red cells until the transfusion of 500 c.c. whole blood. Following this there was no reaction and the patient showed slight blood regeneration. The platelet count steadily increased. No purpuric spots appeared while the patient was in the hospital. Blood transfusion was given on May 16, 1926—500 c.c. whole blood. After transfusion the blood count was:

Hemoglobin	70%
Red blood cells	2,550,000
White blood cells	3,720
Polymorphonuclears	49%
Lymphocytes	32%
Monocytes	16%
Eosinophils	1%

No monoblasts or myelocytes, no basophilia of red cells. Platelets 26,000.

The patient was discharged in June, 1926, improved, with diagnosis of aplastic anemia with purpura. At the time of discharge the blood count was:

Hemoglobin	85%
Red blood cells	3,460,000
White blood cells	6,550
Platelets	68,200

The plant physician reported five months after her discharge from the hospital that her white cell count was between 7,000 and 8,000, that she felt well, and that her condition was good except for the axillary lymphadenitis which did not yield satisfactorily to treatment.

At the end of this investigation when it was evident that a considerable hazard was present, the firm immediately began to experiment with a benzol substitute and has not returned to the use of benzol since that time. Blood counts of most of the affected workers were again made by the factory medical staff at intervals of six weeks, and three months after the removal of the benzol, and showed a progressive improvement. An important point to realize in connection with this plant is that the physical condition of all workers at the time of employment was good. A thorough physical examination before employment weeded out those who were not up to standard requirements.

Factories 3 and 4 both manufactured sanitary tin cans and as they were under the same management with very similar conditions they may be described together. Both were housed in modern buildings where general facilities were good. Both had pleasant lunch rooms and cafeterias. The sanitary tin can industry is the one in which most of the cases of chronic benzol poisoning among women have so far occurred. Benzol is the solvent in a compound used to line or coat a groove around the circumference of the tops and bottoms of cans. This lining acts as a gasket and permits the ends of the cans to be attached to the bodies in an air tight manner. The benzol problem in these factories was known and had received careful study. As a result, a ventilating system for the coating machines had been evolved which appeared to be very efficient. There was no odor of benzol in the room at large and very little was noticeable even in close proximity to the machines. From 20 to 30 gallons of a compound containing 40 per cent. of benzol were used daily in these plants. After coating, the tops were immediately drawn into heated and closed towers and exposed to a strong suction draft. In these towers practically all the benzol evaporated. The chutes upon which the tops emerged were, in one factory, ventilated with a down suction draft and the slatted boxes in which they were packed stood upon racks similarly ventilated in order to draw off any last remaining trace of benzol vapor. The coating

machine operators both tended the machines and packed the tops in one plant. In the other, some tended machines while others packed. Altogether ten women, operators, inspectors, and packers, were examined in these two plants. The complaints among this group were few but in spite of the good ventilation two positive cases of poisoning were found.

Since these examinations were made benzol has been entirely eliminated in these two factories as well as in all others throughout the country which are controlled by the same company.

Factory 5 also manufactured sanitary tin cans and used benzol in its lining compound, but the problem of ventilation had been met in a far less satisfactory manner. There was no direct ventilation of the coated can covers. They emerged from the machine immediately after coating without having been heated and smelling distinctly of benzol. They were then picked up, inspected, and packed in boxes by the women operators. Twelve to eighteen women worked in the room, eight of them in close proximity to the machines. The eight coating machines consumed 45 to 50 gallons daily of a compound containing 75 per cent. of benzol. Underneath each coating machine there was suction exhaust and three exhaust fans were placed, somewhat illogically, in the roof over the machines, but in spite of this the odor of benzol in the room was strong. Adjoining the coating room and connected with it by a wide-open doorway was another room where paper gaskets were made. The odor of benzol in this room, although none was used, was also immediately noticeable. It was discovered that the paper gasket machines were equipped with a suction device to carry off scraps of paper, which was actually stronger than that under the coating machines. Consequently fumes from the coaters, far from being drawn directly away, were carried the length of both rooms, exposing a number of persons to them unnecessarily.

All but three of the fifteen women examined from these two rooms complained of distress such as dizziness, loss of appetite, nausea, and excessive fatigue, associated with the work. The nurse stated that skin rashes among the new employees in the coating room were fairly common and that "quite a few" left because the work made them sick. She told of a girl who had recently given up her job because of attacks of severe abdominal pain which she attributed to the coating compound. Four cases of chronic poisoning were found in this plant. In addition there were three cases in which benzol poisoning was suspected.

One of the girls in this factory told of the death of her sister, also an employee, in June, 1925. No diagnosis of benzol poisoning was made at the time but when the history of the case was obtained from the physician who had treated the girl, the development of the illness and the symptoms appeared so typical that the case was included in the positive group. All the details which could be obtained are given below.

CASE 28.—Age 26. This woman had been employed for some months in the room adjoining the coating machines. She had always been well and was not bothered by the work until she became pregnant. Then she suffered from severe nausea and vomit-

ing. Severe and prolonged nosebleeds began and these were followed by bleeding from the gums and the rectum and into the skin. She stopped work and improved under treatment but against the advice of her physician she then insisted upon returning to work. Purpuric spots recurred. A premature child was born at seven months and three hours after delivery the mother died following a severe uterine hemorrhage.

The increased susceptibility to benzol poisoning accompanying pregnancy, which is illustrated here, is also brought out in several cases mentioned by Hamilton (p. 466).

At their own request four men in this plant who handled benzol were examined. One mixed the compound and the other three worked in the coating room. Three of the four had white cell counts below 5,600.

At the present time the management in this factory is trying, so far as possible, to get away from the use of benzol and has succeeded in eliminating 90 per cent. of it, according to a recent statement.

Factory 6 was a large shoe manufacturing establishment employing about 600 women. When the study was made only three came in contact with benzol and only two actually worked with it. They applied benzol-rubber cement to crêpe rubber soles. In busy seasons five or six women were sometimes employed on this job. The work was done in a large basement with windows on all sides, but these were closed to keep the room comfortably warm. Each worker used about $1\frac{1}{2}$ gallons of cement daily. There was no local exhaust ventilation and the odor of benzol at the end of the room where this work was done was distinctly noticeable. The two cementers were examined and a third woman who worked near by. Both the women who did cementing found that it affected their health. One of them, whose blood picture was normal, had been on the work for only three weeks this season but she had worked at it steadily for the two previous winters. She said that after continuous work for a period of several weeks she felt dizzy and nauseated when beginning work in the morning and would have spells of weakness and palpitation. There was also a distinct tendency to frequent urination accompanied by slight tenesmus. On two occasions she had an itching rash on her hands and forearms. Another woman was interviewed who had done this work a year ago and she also spoke of the tendency to urinate frequently.

Another large shoe manufacturing concern was visited where a fatality had occurred in 1925 from the use of benzol in a cement used for crêpe rubber soles. The hospital records of the case were obtained through the factory medical department and the résumé is given below.

Case 33.—Age 33. This woman was married and had several children. She had been employed for about seven months cementing crêpe rubber soles with a benzol-rubber cement. About the first of May, 1925, she began to feel very listless and weak; nosebleeds began to occur and they became so severe that she went to a specialist for treatment. About the same time purpuric spots are said to have appeared on her skin. She left work May 15 and was admitted to the hospital on June 1. During her stay in the hospital she ran a temperature which usually ranged from about 100° to 102°, occasionally reaching 104°. She had one very severe hemorrhage from the nose and there was bleeding from the vagina. The stools were at times tarry and

she vomited and coughed blood. She complained of weakness, dizziness, nausea, and headache. An abscess of the left thigh developed in the early part of July which opened and drained freely but did not show

TABLE 1.—CASE 33. BLOOD COUNTS

DATE	BLOOD COUNT							
	Hb.	R. B. C.	W. B. C.	Color Index	Polys.	Lymphos.	L. Monos.	Trans.
	%				%	%	%	%
June 4	35	2,240,000	2,400	0.79	39	54	8	3
June 24	25	1,030,000	2,200	1.25	49	40	9	2
July 3	20	860,000	2,016	1.25	65	35	0	0
July 20	17	480,000	3,800	2.1	77	18	4	0
July 31	15	530,000	.....	1.5	..	..	..	..

much inflammatory reaction. The urine showed a slight trace of albumin and a few white and red blood cells. Four transfusions were given on June 11, 19, 23, and July 3 with but slight temporary improvement. The patient died July 31. The blood counts made in the hospital are given in Table 1.

On autopsy the following findings were noted: blood unclotted; marked fatty degeneration of the liver, heart, and pancreas; free blood in the stomach and intestine without evidence of disease of the gastro-intestinal tract; general appearance of anemia. The case was diagnosed as chronic benzol poisoning and compensation was allowed.

The use of benzol cement was promptly abandoned at that time and subsequent experience in this plant has proved that it is not essential to good results.

Discussion of Findings

Percentage of Women Workers Showing Evidence of Chronic Benzol Poisoning

Cases of chronic benzol poisoning occurred in conspicuous porportion in all of the six plants. Of the seventy-nine women exposed to benzol fumes, twenty-five, or 32 per cent., showed blood changes sufficiently marked to indicate clearly that benzol poisoning was present, while in five more, with less marked blood changes, the condition was suspected. Were these cases to be included in the positive group, the percentage of women workers found to be affected by benzol poisoning would be increased from 32 per cent. to 38 per cent. Table 2 indicates the distribution, by factories, of the total number of women exposed to benzol fumes and of the positive cases.

TABLE 2.—WOMEN EXPOSED TO BENZOL FUMES CLASSIFIED BY FACTORY AND EVIDENCE OF CHRONIC BENZOL POISONING

FACTORY	NUMBER EXPOSED TO BENZOL FUMES	NUMBER SHOWING EVIDENCE OF CHRONIC BENZOL POISONING
1. Tire and rubber.....	10	2
2. Photographic supplies.	41	16
3. Sanitary tin cans.....	6	1
4. Sanitary tin cans.....	4	1
5. Sanitary tin cans.....	15	4
6. Shoes.....	3	1
Total.....	79	25

The women who were exposed to benzol fumes may be divided into two classes: those who came into direct contact with benzol through actual use or handling of objects to which it had

been applied, and those whose contact was indirect only and took place merely through working in the same room where it was used. Of the forty-four women in the first group, seventeen, or 38.6 per cent., gave evidence of poisoning; of the thirty-five in the second group, eight, or 22.8 per cent. These figures bring out the fact that working merely in proximity to benzol is attended by a considerable degree of risk.

In this connection it should be mentioned that, although benzol (or benzene) poisoning is included in the New York State Workmen's Compensation Law in the list of occupational diseases for which compensation shall be awarded, the law mentions only processes involving "the use of" benzene and, consequently, the women poisoned through indirect exposure would not be entitled to compensation for time lost on account of their condition. Since they are in all respects as deserving of compensation as those who actually use benzol, the need for a revision in the wording of the Law is obvious.

Analysis of Cases Showing Evidence of Chronic Benzol Poisoning

Table 3 condenses the important data and gives the complete blood counts in the twenty-five positive and the five suspected cases. The three hospital cases already reported, Cases 4, 28, and 33, are not included in this table.

Age.—The ages of all the women examined ranged from 17 to 52 years. The following list shows the age group distribution and indicates the percentage of positive (including suspected) cases found in each group.

Age Group Yrs.	*Total Cases*	*Positive Cases*	
		No.	*%*
17–19	17	2	11.8
20–24	22	10	45.5
25–29	12	6	50.0
30–39	17	6	35.3
40 and over	11	6	54.5

The percentage of positive cases is lowest in the youngest group and highest in the oldest one. While the numbers are too small to be conclusive, youth in this series does not appear to be a predisposing factor in the production of benzol poisoning. It has generally been so considered but this may have been due to the youth of the women exposed in previous studies. In the factory from which Selling's cases came, for instance, all of the fourteen girls exposed at the coating machines were between 14 and 16 years of age, whereas in the factories studied in the present investigation the average age was 28.

Length of Exposure.—The length of exposure among all the women examined ranged from one week to eleven years but in the positive and suspected group the shortest exposure was two months. This was the length of exposure in three instances, Cases 10, 16, and 32. Several women stated that they began to have symptoms such as loss of appetite or nausea almost immediately upon exposure to benzol but it is, of course, impossible to say in these cases how soon chronic poisoning would have been evident from changes in the blood picture. The longest period of exposure in either the positive or the negative group, eleven years, occurred in one of the suspected cases, a coating machine operator. In this instance it is possible that a very mild degree of

TABLE 3.—ANALYSIS OF THIRTY CASES SHOWING EVIDENCE OF CHRONIC BENZOL POISONING OCCURRING AMONG WOMEN EXPOSED TO BENZOL FUMES

CASE NUMBER	AGE	PERIOD OF EXPOSURE	MODE OF EXPOSURE	COMPLAINTS ASSOCIATED WITH EXPOSURE	BLOOD COUNT								
					Hb.	R. B. C.	W. B. C.	Polys.	Lymphos.	Endos.	Eos.	Basos.	Comments
	yrs.				%			%	%	%	%	%	
				Factory 1									
1	17	1 yr.	Uses benzol cement.	Weakness, headache, nosebleeds.	74	4,450,000	5,400	54	40	5	0	1	R. B. C. pale.
2	21	4 yrs.	Works near benzol cement.	Nervousness, dizziness, mental depression, headaches, nausea, weakness, marked fatigue.	70	4,700,000	3,400	43	50	3	2	2	One myelocyte seen.
3[1]	20	18 mos.	Uses benzol cement.	Headache, loss of appetite, marked fatigue, nosebleed.	80	5,300,000	6,200	44	41	6.5	8	0.5	R. B. C. show slight variation in size.
				Factory 2									
5	19	1 yr.	Works in department where benzol cement is used.	Headache, nervousness, weakness, nausea, dizziness, marked fatigue, tingling sensations.	75	4,610,000	5,700	60	25	15	0	0	.....
6	20	3 mos.	Works in department where benzol cement is used	Headache.	75	4,500,000	5,400	46	45	5	4	0	.....
7	26	5 yrs.	Uses benzol cement.	Headache, dizziness, nosebleeds, tingling sensations, frequent urination.	66	3,650,000	4,820	42	46	12	0	0	Occasional myelocytes. R. B. C. show variation in size.
8	29	10 mos.	Works in department where benzol cement is used.	Dizziness, marked fatigue, numb sensation in hands, frequent urination.	76	4,210,000	5,800	64	20	15	1	0	R. B. C. show variation in size and staining.
9	30	4 yrs.	Works in department where benzol cement is used.	Nervousness, excessive fatigue, inability to sleep, headaches, loss of appetite.	75	3,450,000	4,600	60	27	11	2	0	Occasional myelocytes. R. B. C. pale, show variation in size and shape.
10	32	2 mos.	Uses benzol cement.	More frequent menstruation.	68	5,000,000	3,800	41	45	9	5	0	.....
11	25	4 yrs.	Works in department where benzol cement is used.	Fatigue, poor appetite, headaches.	73	4,550,000	4,500	56	28	13	1	1	Occasional myelocytes. Slight variation in size and shape of R. B. C.
12	38	4 yrs.	Works in department where benzol cement is used.	Indigestion, nausea, poor appetite, headache, inability to sleep, dizziness, nervousness.	67	3,710,000	5,600	44	40	3	13	0	Occasional myelocytes. R. B. C. show slight variation in size.
13	40	4 yrs.	Uses benzol cement.	Nervousness, headache, dizziness, fatigue, inability to sleep, numb sensation in hands, frequent urination.	63	4,160,000	5,000	37	53	10	0	0	R. B. C. pale.
14	43	3 yrs.	Uses benzol cement.	Fatigue, dizziness, weakness, indigestion, nausea, skin eruptions.	73	3,140,000	5,200	54	25	19	2	0	Occasional myelocytes. R. B. C. show variation in staining.
15	46	4 yrs.	Works in department where benzol cement is used.	Fatigue, weakness, dizziness, indigestion, numb sensations in hands, frequent menstruation.	76	3,630,000	5,200	58	33	7	1	1	Occasional myelocytes. R. B. C. show slight variation in size and staining.

16	23	2 mos.	Sprays lacquer containing benzol.	None.	66	4,660,000	5,000	49	45	3	1	2	.....
17	29	4 yrs.	Sprays lacquer containing benzol.	Headache, nausea, marked fatigue, weakness, nervousness, indigestion.	85	5,670,000	5,000	32	62	5	1	0	Occasional myelocytes.
18	22	3 mos.	Sprays lacquer containing benzol.	Loss of appetite, nausea, marked fatigue.	67	4,420,000	4,100	60	23	11	4	2	R. B. C. pale, show slight variation in shape and staining.
19	27	16 mos.	Sprays lacquer containing benzol.	Nausea, dizziness.	67	4,500,000	5,500	50	41	8	1	0	.....
20	22	8 mos.	Sprays lacquer containing benzol.	Loss of appetite, dizziness.	70	4,490,000	4,800	63	25	10	2	0	.....
21[1]	42	4 yrs.	Works in department where benzol cement is used.	Fatigue, weakness, dizziness.	80	3,760,000	6,800	52	39	9	0	0	Occasional myelocytes. R. B. C. show variation in size.
				Factories 3 and 4									
22	38	1 yr.	Coating machine operator.	Shortness of breath.	67	3,640,000	5,000	.....	.....	.....	.....	.....	.....
23	49	4 yrs.	Packs coated can covers.	Headache, dizziness.	63	3,260,000	3,200	55	36	4	5	0	Occasional myelocytes. R. B. C. show slight variation in size.
				Factory 5									
24	20	4 yrs.	Works in coating room.	Headaches, nosebleeds.	65	3,330,000	5,445	69	21	6	2	1	Few myelocytes. R. B. C. show slight variation in size and shape.
25	20	2½ yrs.	Works in coating room.	Headaches.	70	4,450,000	4,450	54	37	3	3	2	Few myelocytes and Türck's irritation leukocytes. R. B. C. show variation in size.
26	20	4 mos.	Works in coating room and room adjoining.	Fatigue.	75	3,700,000	5,650	67	28	1	2	1	One Türck's irritation leukocyte.
27	38	6 yrs.	Works in coating room and room adjoining.	Loss of appetite, pain in the epigastrium, nausea, excessive fatigue, weakness, loss of weight.	.....	4,310,000	5,000	63	30	2	4	0	Few myelocytes. R. B. C. pale.
28[1]	30	11 yrs.	Coating machine operator.	Headaches, nausea, loss of appetite, pain in the epigastrium, vomiting, disturbed sleep, loss of weight, shortness of breath, frequent urination.	65	3,430,000	6,150	65	28	7	0	0	Few myelocytes. R. B. C. pale and show variation in size.
29[1]	46	3 yrs.	Works in coating room and room adjoining.	Headaches, extreme dizziness, nausea, vomiting, rash on leg.	.....	3,770,000	6,400	.....	.....	.....	.....	.....	.....
30[1]	21	2 yrs.	Inspects coated can covers.	Menstruation prolonged and frequent, headaches, loss of appetite.	.....	4,440,000	6,100	59	35	2	3	1	Few myelocytes. R. B. C. pale.
				Factory 6									
31	25	2 mos.	Uses benzol cement.	Headaches, drowsiness.	75	5,100,000	4,800	45	52	1	0	2	Myelocytes.

[1] Indicates suspected cases.

chronic poisoning had been present for a long time. The woman in question had not felt really well since beginning work; her appetite had never been very good and she had lost weight progressively.

The following list indicates the distribution of cases according to length of exposure:

Length of Exposure	*Total Cases*	*Positive Cases*	
		No.	%
Under 3 mos.	20	3	15.0
3–12 mos.	12	5	41.7
1–4 yrs.	19	9	47.4
4 yrs. and over	28	13	46.4

The percentage of positive cases is lowest in the group with an exposure of three months or less but shows little difference among the other three groups. This would seem to indicate that where susceptibility to poisoning exists it tends to develop during the first year though, of course, other factors such as severity of exposure, which cannot be evaluated, enter into the result.

Appearance.—In general these women quite definitely did not look well. The outstanding characteristics were a look of fatigue and pallor; the latter, though not invariably found, occurred in the majority and was striking when present. Some women with a history of long exposure looked prematurely aged; a few were underweight to the point of emaciation. The proportion of overweight individuals in the positive group as a whole, however, was larger than in the negative group and only a few complained of loss of weight. Good nutrition, evidently, is not incompatible with chronic benzol poisoning, at least in the early stages. Two questionable purpuric spots were found on the forearm of one woman, a bellows cementer, who thought they had occurred spontaneously, and petechiae were present on the arms and neck of another. No other skin lesions possibly attributable to benzol were found at the time of examination.

Blood Pressure.—The blood pressure did not show anything of particular interest. The average systolic pressure was low (about 115) in both groups, as might be expected in a class of sedentary indoor workers, but was not noticeably lower in the positive than in the negative group.

Symptoms.[1]—Spectacular symptoms, such as bleeding from the mucous membranes or purpura, were conspicuously absent from this group of women still at work who in many cases did not realize that anything out of the ordinary was wrong with their health. But the frequency with which less striking complaints occurred among them was impressive and significant. This was true to a large extent also among the women exposed to benzol but not included in the positive or suspected group. The symptoms which were found among the latter group are shown in the order of frequency in Table 4.

In questioning the women regarding various symptoms, an effort was always made to determine whether or not the complaint in question had

[1] Data as to whether or not women are more susceptible than men to benzol poisoning were not secured since in no case were groups of opposite sexes found working under similar conditions. That women may suffer more from subjective symptoms than men having an equal degree of leukopenia, is suggested by records secured from Factory 2, which showed that of fifteen men exposed to benzol vapor, whose white cell counts were below 5,625, only one had symptoms associated with the work.

developed after exposure to benzol or, if it had been present previously, whether it had increased in frequency or severity since exposure. Complaints were recorded only when such an apparent relation to exposure was present.

It is known that blood changes may occur in chronic benzol poisoning unaccompanied by symptoms. This was illustrated by only one case in this series where the white cell count was 5,000 while the woman made no complaint. The highest number of listed complaints made by any one person was eight; the average number of complaints per person was a little over three.

Headaches, the commonest complaint, occurred among 60 per cent. of the women in the positive and suspected group. Their frequency varied from "almost every day" to "two or three times a month." They tended to be more frequent in winter and to increase in severity as the day wore on. In some cases they would persist steadily for several days; one woman when interviewed said that she had had a headache for "three days straight." Sometimes the headaches were accompanied by nausea and dizziness.

Excessive fatigue was complained of by 46.7 per cent., almost one-half, of these women. Distinction was made between ordinary fatigue to be expected after a day's work and a feeling of exhaustion, of being "all in." The women who replied in the affirmative believed that they got abnormally tired; some said they felt tired "all the time." This finding has the more significance because in the majority of cases the work was not especially arduous and only seven of the thirty women were obliged to stand continuously at their jobs.

TABLE 4.—FREQUENCY OF COMPLAINTS AMONG WOMEN SHOWING EVIDENCE OF CHRONIC BENZOL POISONING

COMPLAINT	TOTAL CASES	
	Number	Per Cent.
Headache	18	60.0
Excessive fatigue	14	46.7
Dizziness	13	43.3
Nausea	10	33.3
Anorexia	9	30.0
Weakness	8	26.7
Nervousness	6	20.0
Numbness and tingling	5	16.6
Frequent urination	4	13.3
Nosebleeds	4	13.3
Disturbed sleep	4	13.3
Indigestion	4	13.3
Frequent menstruation	3	10.0
Shortness of breath	2	6.7
Skin eruptions	2	6.7
Vomiting	2	6.7
Pain in abdomen	2	6.7

About 43 per cent. complained of spells of dizziness. These occurred for the most part while at work though one woman noticed that she felt more dizzy on going home. One coating machine operator said that she became so dizzy at times that she felt "drunk." Several women noticed a connection between dizziness and closed windows or the opening of fresh cans of cement.

About 33 per cent. felt nauseated, "sick to the stomach," at times while at work. This feeling was more apt to occur when first beginning work in the morning. A number of the women said that they had felt nauseated for the first few days after exposure to

benzol had begun but that the feeling gradually wore off as they became accustomed to the odor. In one plant it was a fairly common thing, according to the nurse, for new employees to leave because "the work made them sick." Anorexia or indifference to food occurred among 30 per cent. of the women and in most cases dated rather definitely from the time of beginning work. Four women complained of "indigestion" which may or may not have been related to benzol absorption. Spells of actual vomiting had occurred during the previous few months in two of the suspected cases (29 and 30). These women were both coating machine operators employed in the same factory; one had a history of eleven and the other of three years' exposure. Both had numerous other complaints including, in the case of one, pain in the abdomen, and both appeared to be in poor shape. Neither, however, had a marked reduction in the white blood cell count. Pain in the epigastrium described as "pursing," occurred in the case of one other woman (Case 27) with a history of six years' exposure. She complained as well of weakness, excessive fatigue, loss of weight, nausea, and loss of appetite.

A feeling of weakness, of general muscular inefficiency, occurred in eight, or 26.7 per cent., of the cases. This may have been associated with excessive fatigue since all but one of the women making this complaint also complained of fatigue. However, six of those who complained of fatigue did not complain of weakness.

Evidences of the neurotoxic action of benzol as seen in disturbances of sensation, chiefly in the extremities, were present in five cases, 16.6 per cent. These women noticed on occasions sensations of numbness or tingling in their hands, arms, legs, and feet. Such sensations were more marked when holding objects or when maintaining a constant position. The same complaint was also present among a large percentage of the women who were exposed to benzol but whose blood did not show marked changes. Six women complained of "nervousness." In one, it was associated with extreme dizziness and took the form of mental depression and confusion which at one time necessitated a sick leave of several weeks. Another felt "nervous" at the same time that severe headaches occurred which were also accompanied by dizziness, nausea, and weakness. In a third, nausea and nervousness were associated; while a fourth "lost control" of herself easily. Four who also suffered headaches complained of wakefulness at night.

Frequent urination which was mentioned by Starr as a common symptom among the milliners whom he examined and attributed by him to the possible excretion of phenols in the urine, but which has not been emphasized by other investigators as a symptom of chronic benzol poisoning, was one of the complaints of four women whose blood pictures were positive. Two more who had worked with benzol previously stated that this symptom was definitely associated with its use and developed after a few weeks' continued exposure. It was not constant but would come and go for periods of a few days at a time. One woman described a sensation which

was evidently a slight tenesmus associated with the frequency.

Only a few complaints were made of dermatitis attributable to benzol. One coating machine operator said that the work was apt to cause an itching rash to appear on her legs and sometimes on her thighs and forearms. A cement worker whose blood picture was negative had had a similar rash on her hands and forearms on several occasions and another was troubled in the same way when she used benzol for cleaning. Two girls who worked in the tire department of the rubber factory had had attacks of furunculosis which in one were more prone to occur in the warm weather.

With regard to bleeding, one girl (Case 1) had been having nosebleeds during the week immediately prior to the interview, while three others had had them on one or more occasions in the past while working with benzol. No mention was made of bleeding from the gums except upon cleaning the teeth, a symptom probably without significance. None of the women complained of purpuric spots and there was some question as to the authenticity of those found in Case 14. They were, however, a conspicuous feature in the three hospital cases. In the two cases which terminated fatally there was bleeding from all the mucous membranes. The menstrual function in the majority of positive and suspected cases was undisturbed. The most conspicuous irregularity which might be attributed to benzol occurred in a suspected case (Case 31), a coating machine operator. She had had periods occurring every two weeks for the past four months with profuse bleeding lasting five to seven days. A similar condition had occurred once before about a year previously but had ceased when she gave up work for a while. In spite of the very considerable loss of blood her red blood cell count remained high. The white blood cell count was 6,100. In two other instances the benzol effect may have been evident in the fact that the interval between periods had diminished from four to three weeks since exposure, though the flow was not noticeably freer. In one case, menstruation which had formerly been scanty became more profuse, though not unduly so, after taking the job involving exposure to benzol; in another, periods which had been occurring once in two or three months began to occur regularly. Whether there was any connection between these changes and exposure to benzol it is impossible to say since other unknown factors may have been present. A number of women spoke of headaches and dizziness being more pronounced at the menstrual period.

In addition to the symptoms occurring in the positive and suspected cases, the numerous complaints made by those whose cases were considered presumably negative because their white cell counts were not conspicuously reduced cannot be ignored. A large proportion of these workers, about 39 per cent., had symptoms associated with their work. The proportion making complaints differed in the various factories and was smallest in those where artificial ventilation reduced the air contamination, as it did in Factories 3 and 4. Thirty-one per cent. of these so-called negative

cases showed complaints of dizziness, 29 per cent. of excessive fatigue, 25 per cent. of headaches, 16 per cent. of nausea, 10 per cent. of weakness, 8 per cent. of loss of appetite. In a conspicuous number, signs of nerve irritation, *i. e.*, mild disturbances of sensation in the extremities, were present. It is, of course, possible that in a number of cases these complaints arose from other causes than benzol, yet their nature and frequency make it seem probable that these women also were being affected by the inhalation of benzol fumes to the detriment of their efficiency and well-being. Moreover, a certain number of the cases showed some variations from the normal blood picture which will be discussed later. These, together with the occurrence of symptoms connected with exposure to benzol, suggest that possibly the standard by which these cases were considered negative, namely, failure to show a 25 per cent. reduction in the white count, was too arbitrary. It is possible that some of them at least showed an earlier manifestation of the benzol effect than did those having a typical leukopenia, and that they should rightly be included among the cases of chronic benzol poisoning.

Blood Counts.—The blood changes in the thirty cases in which evidence of chronic benzol poisoning was found are not startling in comparison with the blood pictures shown in advanced stages of poisoning, but they show unmistakable evidence, especially in the white and differential counts, that a pathologic condition of a serious nature is in progress.

Hemoglobin was moderately reduced in all but three cases; the lowest percentage found was 63, the highest 85, a normal amount, and the average about 71. Severe anemia seems to develop only in the later stages after bleeding has commenced. Thus one of the fatal reported cases showed a hemoglobin of 15 per cent. before death. Case 4 in which purpuric spots but no bleeding from the mucous membranes had developed, had a hemoglobin of 70 per cent.

The *red blood cells* as well as the hemoglobin show, as might be expected, much less relative reduction than the white cells. Destruction of the red cells has been said to be the last change to appear and the last to disappear in benzol poisoning. In this series no counts were lower than 3,000,000.

Number of Red Cells	*Distribution of Cases*
3,000,000—3,500,000	5
3,500,000—4,000,000	7
4,000,000—4,500,000	8
4,500,000—5,000,000	6
5,000,000—5,700,000	4

It is known that the earliest effect of benzol absorption or the effect of the absorption of small amounts is sometimes an actual stimulation of the blood forming organs resulting in an increase in the red and sometimes in the white corpuscles. With this in mind it is interesting to note that Cases 3, 17, and 32 each showed red blood cell counts above 5,000,000. Among the negative cases, moreover, eleven, or 22 per cent., in all of which symptoms were present, showed an increase in red cells without a corresponding increase in hemoglobin. It seems possible, therefore, that these cases should be considered cases of benzol absorption or very early cases of chronic poisoning.

No increase in *bleeding time* was

observed in the majority of these cases. In several instances, however, bleeding from the prick was abnormally prolonged. *Coagulation time* was not taken. A record was obtained from the medical department of Factory 2, however, of the coagulation time in fifteen men benzol workers in whom there was a leukopenia of 5,625 or below. In none of these cases was it prolonged.

The *color index* in this series ranged from 0.7 to 1.5, while the average was 0.8. A higher index is apt to occur in the more advanced cases where red blood cell destruction is severe. In Case 33, for example, the color index ranged from 0.7 on admission to the hospital to 2.1 a few days before death.

The *white blood cell counts* in the positive cases ranged between 3,200 and 5,600 with three exceptions as against the normal of 7,500; in the five suspected cases between 6,100 and 6,800. Their distribution is indicated in the following list:

Number of White Cells	*Distribution of Cases*
3,000—3,500	2
3,500—4,000	1
4,000—[illegible]	2
4,500—5,000	5
5,000—5,600	11
5,600—6,900	9

The significance of this white cell reduction lies in the diminished resistance to infection which it entails. The normal defensive power against disease of each of these workers has been lessened through the circumstances of her work. An illustration of this diminished resistance to infection is furnished in Case 4 where the white cells were reduced to 3,600. After apparent recovery and discharge from the hospital an infection of the lymph nodes under the arm persisted for months in spite of treatment, and with this condition there was a failure, due in all probability to bone marrow damage, to produce the leukocytosis which represents the normal reaction to infection. Case 33 also illustrates this complete inability to rally the leukocytes; when an abscess of the thigh developed in this case the leukocyte count increased from 2,000 to only 3,800.

Fully as important as an enumeration of the leukocytes in these cases is a careful study of the stained blood smears to show whether any normal cells are abnormally prevalent or whether any abnormal cells occur. Variations from the normal *differential count* give a more vivid picture of the damage in progress than the mere reduction in the number of the leukocytes.

A diminution in the percentage of the polymorphonuclear leukocytes (neutrophils) is generally reported as characteristic of chronic benzol poisoning. In this series there was such a tendency. The average percentage of the polymorphonuclear cells was 53 as against the normal 60 to 70, but a reduction in percentage was not invariably shown. A number of cases with marked leukopenias showed a normal percentage of polymorphonuclears. It is possible, of course, that this may have been the result of some unknown focus of infection. On the other hand, many of the negative cases with normal white cell counts showed a diminution in the percentage of polymorphonuclears. The reason for

this is obscure unless it is associated with the confining, unhygienic life of the factory worker.

One variation from the normal which appeared in almost half the cases was the increase in the endotheliocytes (by some called monocytes), a term now widely used to include cells formerly known as large mononuclears and transitionals. These cells normally constitute from 2 to 6 per cent. of the total number of leukocytes. Fifteen out of twenty-eight, or 53.5 per cent., showed an increase above 6 per cent. which in one instance reached as high as 19 per cent. One of the reported cases (Case 4) had an endotheliocytosis of 27 per cent. at one time, and in the reported fatality (Case 33) 11 per cent. of endotheliocytes were present. In the literature on benzol poisoning mention is made of an increase in both large mononuclear and transitional cells. In two of Selling's cases, large mononuclear cells constituted 14 and 10 per cent. of the total number of white cells and Hamilton mentions two cases reported by Brücken where increases to 10 and 12 per cent. occurred. In McClure's case the transitional cells numbered 15 per cent. The significance of endotheliocytes, *i. e.*, large mononuclear and transitional cells, is not clearly understood. Todd states that some at least are developed from the lining cells of the blood and lymph vessels. An increase occurs in a number of pathologic conditions, notably typhoid fever, malaria, and Hodgkin's disease. Minot and Smith (cited by Todd) have demonstrated an increase in endotheliocytes in tetrachlorethane poisoning.

An abnormal increase in the type of white cells known as eosinophils was present in Cases 3 and 12. An eosinophilia in benzol poisoning, according to Hamilton (p. 477), has been found by several European investigators.

The basophils or mast cells which ordinarily are present to the extent of one in 200 or 300 showed a slight tendency to increase 1 or 2 per cent. in a fairly large number of the positive and suspected cases and in a few of the negative group. These cells originate in the bone marrow and when present in increased amounts are indicative of bone marrow irritation. The same thing is true of Türck's irritation leukocytes which were present in two cases.

The variety of white cell known as a myelocyte, which is never present in normal blood, was seen in more than 50 per cent. of these blood smears. This cell is the bone marrow predecessor of the polymorphonuclear leukocyte. A few of them may occur, according to Todd, in any severe blood condition and Krumbhaar states that leukopenia caused by inhibition or intoxication of the bone marrow is followed by the appearance of very immature leukocytes in the blood stream. The fact that myelocytes, evidences of bone marrow intoxication, were found in three cases (Cases 21, 29, and 31) where the leukopenia was not marked, the white cell count being between 6,000 and 7,000, shows that a 25 per cent. reduction in the white count should not be used as the only criterion of poisoning.

The appearance of the red cells in the stained smears was in general

indicative of anemia. Polychromatophilia, or differences in staining of cells in the same slide, was present to some extent. This is usually considered indicative of young, immature corpuscles. There was also a considerable amount of anisocytosis, or variation in size, with the presence especially of larger forms than normal; in a few slides slight variations in shape were noted.

Summarizing the blood examinations, then, it may be said that evidence of a pathologic condition was shown by the anemia, the appearance of the red cells, the reduction in white cells, the presence of abnormal cells such as myelocytes and Türck's irritation forms, and the abnormal increase in endotheliocytes.

Improvement in Blood Counts Following Removal of Benzol

In Factory 2 it was possible to secure follow-up blood counts which were made on most of the positive cases after the elimination of benzol. These give an indication of the rate at which improvement took place in these cases. Of fifteen cases in which a blood count was repeated at the end of six weeks, the white cell count showed a definite improvement in seven, a slight improvement in three, and no improvement in five, or 33.3 per cent. The differential count, however, had either returned to normal or was improved in all but one case. Seven of these fifteen cases had red cell counts lower than 4,500,000. At the end of six weeks three showed no change, one was improved, and three had returned to normal. Blood counts made at the end of three months showed that out of eleven cases three still had a leukopenia. Of the five cases in which the red cell count had been reduced, three had returned to normal and two were improved.

Summary

1. Benzol as used in the industries investigated produced chronic poisoning in virtually one out of every three women.

2. The risk of poisoning was not limited to those who worked directly with benzol; but workers who were indirectly exposed through merely working in rooms where benzol was used were also subject to its effect.

3. Among women who did not show definite signs of poisoning more than one-third suffered from symptoms many of which in all probability were caused by exposure to benzol.

4. Susceptibility to benzol poisoning appeared about equally marked among young and older workers.

5. The commonest symptoms accompanying blood changes indicative of early chronic poisoning among the women examined were headache, excessive fatigue, dizziness, nausea, loss of appetite, weakness, nervousness, and disturbances of sensation such as numbness and tingling in the extremities. Frequent urination, nosebleeds, disturbed sleep, and indigestion occurred in about 13 per cent. of the cases; menstrual irregularities, in about 10 per cent.

6. The blood showed in addition to leukopenia and a tendency toward a diminution in the polymorphonuclear leukocytes—the commonly accepted criteria of chronic benzol poisoning—a tendency toward a slight increase

in basophils, as well as an increase in the endotheliocytes and the presence of myelocytes in a noteworthy number of cases.

7. Reports were obtained of three cases which had advanced to the point of hospitalization. Two of these were fatal.

BIBLIOGRAPHY

1. Anderson, H. B., Boyd, J. S., and Jackson, A. B.: A Series of Cases of Purpura Haemorrhagica and Aplastic Anaemia Due to Chronic Benzol Poisoning in a Canning Plant. Canadian Med. Assn. Jour., 1923, *13*, 395.
2. Bull. N. Y. State Indust. Comm., 1920, *6*, 20.
3. Burnet, J.: Industrial Benzene Poisoning. Clin. Jour., 1918, *47*, 152.
4. Duke, W. W.: Causes of Variation in the Platelet Count. Experimental Results Showing the Effect of Diphtheria Toxin, Benzol and Tuberculin on the Platelet Count in Rabbits. Arch. Int. Med., 1913, *11*, 100.
5. Final Report of the Committee on Benzol. Nat. Safety Council, May, 1926.
6. Glaser, C.: Investigation into Several Cases of Poisoning by Vapors of "C. P." Benzol. Bull. Johns Hopkins Hosp., 1911, *22*, 8.
7. Hamilton, A.: Industrial Poisons in the United States. New York, The Macmillan Co., 1925.
8. Harrington, T. F.: Industrial Benzol Poisoning in Massachusetts. Boston Med. and Surg. Jour., 1917, *177*, 203.
9. Hektoen, L.: The Effect of Benzene on the Production of Antibodies. Jour. Infect. Dis., 1916, *19*, 69.
10. Hogan, J. F., and Shrader, J. H.: Benzol Poisoning. Am. Jour. Pub. Health, 1923, *13*, 279.
11. Howe, H. E.: Chemistry in Industry. New York, The Chemical Foundation Co., Inc., 1924.
12. Hurwitz, S. H., and Drinker, C. K.: The Factors of Coagulation in the Experimental Aplastic Anemia of Benzol Poisoning, with Special Reference to the Origin of Prothrombin. Jour. Exper. Med., 1915, *21*, 401.
13. Kline, B. S., and Winternitz, M. C.: Studies upon Experimental Pneumonia in Rabbits. V. The Rôle of the Leucocyte in Experimental Pneumonia. The Relation of the Number of Organisms Injected to the Mortality. *Ibid.*, 1913, *18*, 50.
14. Krumbhaar, E. B.: Leukemoid Blood Pictures in Various Clinical Conditions. Am. Jour. Med. Sc., 1926, *172*, 519.
15. Legge, T. M.: Chronic Benzol Poisoning. This Jour., 1919–1920, *1*, 539.
16. McClure, R. D.: Pernicious Anemia Treated by Splenectomy and Systematic, Often-Repeated Transfusion of Blood. Transfusion in Benzol Poisoning. Jour. Am. Med. Assn., 1916, *67*, 793.
17. Molinari, E.: Treatise on General and Industrial Organic Chemistry. Philadelphia, P. Blakiston's Son & Co., 1921, p. 630.
18. Newton, C. R.: Industrial Blood Poisons. Jour. Am. Med. Assn., 1920, *74*, 1149.
19. Occupation and Health. Brochure No. 8: Benzene (Benzol). Geneva, International Labour Office, 1925.
20. Reifschneider, C. A.: Benzol Poisoning. Its Occurrence and Prevention. Proc. Nat. Safety Council, 1922, p. 249.
21. Rusk, G. Y.: Studies on the Locus of Antibody Formation. II. The Effect of Benzol Intoxication and Consequent Leucopenia on the Formation of Artificial Hemolysins and Precipitins. Univ. Calif. Pub. in Path., 1914, *2*, 139.
22. Selling, L.: Benzol as a Leucotoxin. Studies on the Degeneration and Regeneration of the Blood and Haematopoietic Organs. Johns Hopkins Hosp. Rep., 1916, *17*, 83.
23. Selling, L.: A Preliminary Report of Some Cases of Purpura Haemorrhagica Due to Benzol Poisoning.

Bull. Johns Hopkins Hosp., 1910, *21*, 33.

24. Starr, E. B.: Poisoning by Benzol Carbon Tetrachloride Cement, with Special Reference to the Early Symptoms of Benzol Poisoning. This Jour., 1922–1923, *4*, 203.
25. Todd, J. C.: Clinical Diagnosis by Laboratory Methods. A Working Manual of Clinical Pathology. Philadelphia, W. B. Saunders Co., 1925, p. 312.
26. Underhill, F. P., and Harris, B. R.: The Influence of Benzol upon Certain Aspects of Metabolism. This Jour., 1922–1923, *4*, 491.
27. Weiskotten, H. G., Gibbs, C. B. F., Boggs, E. O., and Templeton, E. R.: The Action of Benzol. VI. Benzol Vapor Leucopenia (Rabbit). Jour. Med. Res., 1919–1920, *41*, 425.
28. Weiskotten, H. G., and Steensland, H. S.: The Action of Benzol. IV. Spontaneous Infection with Special Reference to the Diphasic Leucopenia (Rabbit). *Ibid.*, 1917, *37*, 215.
29. White, W. C., and Gammon, A. M.: The Influence of Benzol Inhalations on Experimental Pulmonary Tuberculosis in Rabbits. Tr. Assn. Am. Phys., 1914, *29*, 332.
30. Winternitz, M. C., and Hirschfelder, A. D.: Studies upon Experimental Pneumonia in Rabbits. Parts I to III. Jour. Exper. Med., 1913, *17*, 657.

THE PHYSIOLOGY OF INDUSTRIAL HYGIENE: II. THE PHYSIOLOGIC EFFECTS OF EXERCISE AND MENTAL EFFORT ON THE CIRCULATION, AND THEIR RELATION TO INDUSTRY*

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ATTENTION was drawn in a previous paper (1) to the fact that in exercise a primary consideration is an adequate supply of blood to the active part; it may be at the expense of the supply to other parts, such as the alimentary canal. Our present consideration is how far this adaptation may vary and may influence industrial work. In the first instance it will be profitable to consider in more detail the actual circulatory adaptations which take place in muscles.

For convenience we may divide the adaptations to exercise into two categories: those which originate in the active muscles themselves directly or indirectly, and those more dependent on impulses from the higher mental mechanisms.

When a muscle contracts there are brought into operation several mechanisms by which the muscle improves its own blood supply. At rest only a relatively small number, in an average muscle about an eighth, of the capillaries are open, the remainder are closed (Krogh), but when the muscle becomes active many of the capillaries are brought into use. The cause of this opening up, we have good reason to believe from the work of Hemingway and McDowall (2), is lactic acid which is produced in activity, especially when the contraction takes place anaërobically or at least when the supply of oxygen is insufficient, as it presumably is before the capillaries open up. Once there is an adequate supply of oxygen, we may understand from the work of Severini, Bayliss (3), and others that carbon dioxide is responsible for the maintenance of dilatation.

The larger arterioles to the part which, because of their thick walls, are in less immediate contact with the active tissues, we believe are opened up by reflex mechanisms akin to the reflexes of Loven. This observer found that, if the afferent nerve from an organ be stimulated, there is brought about dilatation in that organ and a shutting down of other areas not in use. It seems likely that during exercise afferent fibers from the active muscles bring about a similar local dilatation and general constriction, but indisputable evidence on this point is still lacking although of recent years it has been demonstrated that afferent fibers from the limbs capable of causing dilatation of vessels do exist (Vincent).

The muscles also bring about a constriction of vessels in unused regions, through the influence of the

* Received for publication Nov. 18, 1927.

carbon dioxide they produce, upon the vasomotor center, which has been shown by Dale and Evans (4) to be stimulated by this acid. This effect of carbon dioxide may readily be shown experimentally in a constriction of the splanchnic vessels and those of the skin. As a result of the constriction a larger amount of blood becomes available for the muscles and the venous pressure is raised. The muscles themselves further contribute to the venous return by their compression of the valvular veins of the limbs, which only allow blood to flow centrally. In addition, the increased action of the respiratory mechanism (5), as well as the result of increased carbon dioxide produced by the muscles, still further facilitates the return of blood to the thorax.

We have then a variety of mechanisms which greatly increase the filling of the heart and thereby increase its output per beat. This occurs in virtue of Starling's "law of the heart," which indicates that the more the heart is filled by the end of the diastole, the more forcibly it contracts. At the same time the heart rate increases, further increasing the output per minute. This increase is due, in part, to the raised temperature of the blood leaving the active muscles and, in part, to the raised venous pressure. This latter acts directly on that area of the right auricle, the pacemaker, responsible for controlling the rate of the heart; at the same time the Bainbridge (6) reflex is brought into operation. By this reflex there is, as a result of impulses passing up the vagus, a reduction of the normal vagus restraint of the heart and increased sympathetic action.

The total effect of the increased cardiac output and the vasoconstriction is, in spite of the local dilatation, a rise in blood pressure which may be raised to double the normal; a fact which, there seems little doubt, is of paramount importance in insuring an adequate supply of blood wherever it is required.

In relation to industry it should be pointed out that the mechanisms which have been described are controlled by the vasomotor system, the activity of which varies according to the normal habits of the individual. We know, for example, that in persons accustomed to severe physical exercise the vagus restraint of the heart is greater than in those engaged in sedentary occupation and the former may be considered to have a greater range of adaptability. Similarly, the vasomotor systems of caged animals, *e.g.*, rabbits, are usually less efficient than those of animals in the wild state. We know also that, after a long period in bed, we become specially liable to giddiness on assuming the erect posture. Further, if muscles are not utilized we may presume that they do not become flushed as they ought and deleterious products will tend to accumulate. These facts suggest that a period of absence from work actually renders an individual physically less capable of work and no doubt all the more liable to suffer from fatigue and distaste of work. They tend to show also that any system of dole without work is fundamentally unsound from the physiologic point of view. This matter will be

dealt with in a subsequent paper on the subject of fatigue. It becomes evident then that, just as was stated in relation to the alimentary canal, there is, as is apparent from the cardiac acceleration and vasoconstriction, increased sympathetic and diminished parasympathetic (*e.g.*, vagus) action.

What has been written above has referred to the effects of adaptation to exercise once it has begun. Actually we know that many of the changes described have begun before the exercise and while the individual was merely contemplating the activity, and even at this stage there is increased cardiac action and vasoconstriction which result in a rise in blood pressure as a result of impulses which pass down from the higher cerebral areas.

We have remarked in relation to the alimentary canal that there is a definite physiologic reaction during certain mental states, but it is also evident that a similar purposeful reaction occurs in regard to the circulation. At the present stage we may simply note that it is agreed in industry that the mental attitude of the workers is of the greatest importance.

It has long been known that any form of mental attention or effort is associated with definite changes in the circulation. Mosso (7) in some of his earliest experiments demonstrated a diminution in the blood volume of the limbs during mental effort, indeed, this was the first experiment ever done by Mosso with the plethysmograph. He claimed also that there is a definitely increased blood flow through the head. The former observation is quite easy to confirm. It is well known that the heart rate and the blood pressure may be increased by purely mental effort (8). Leonard Hill has previously recorded a similar change consequent on the giving of a lecture. The writer has found that under such circumstances the blood pressure may rise from 110 to 160.

The observations of clinicians are also of interest in this respect. Lord Dawson (9) has recently pointed to a raised blood pressure in a considerable proportion of schoolchildren preparing for examinations and it is suggested that mental stress may be responsible for many cases of high blood pressure, which is a common feature of modern life. It is, however, not claimed that all cases of hyperpiesis are so produced, but it is well recognized clinically that retirement from an active life will result in an appreciable reduction in blood pressure. It has also been observed that in many cases of blood pressure there are periods of normality indicating that the increase has been produced by an active vasoconstriction rather than by a permanent reduction in the arterial lumen. MacWilliam (10) has also pointed out that death during sleep is commonly due to a rise in blood pressure during emotional dreams. How far a rise in blood pressure so produced may eventually lead to arterial disease is a matter of debate, but certain it is that a considerable amount of extra work is thrown on the heart and may result in the failure of that organ.

That severe and prolonged mental stress is eventually harmful there appears to be little doubt, but it is just as evident that the circulatory change is a normal reaction and that many individuals do not suffer in any way from lives of great mental activity; indeed, they are often blessed with

long life. We must presume that individuals differ appreciably in the extent to which they can relax, particularly in sleep, a fact which appears to depend on their mental make-up. Some leave their worries at the office door, while others not only take theirs home, but also dream of them. A characteristic of excessive mental activity appears to be that it can be maintained indefinitely; whereas severe muscular activity is less likely to be kept up because of the physical fatigue which ensues and acts as a safeguard. We should, however, note that severe and prolonged physical work is commonly associated with persistent high blood pressure (Osler).

The other side of the question of high blood pressure must also be considered in some detail; namely, the extent to which circulatory reaction may contribute to efficiency, the more so as we know that increased function is usually purposeful. In industrial life it is, as we have said, well recognized that interest bears a definite relation to output; also, from work carried out in this laboratory on the skin circulation, it appears that interest in the task has similarly some relation to the amount of vasoconstriction which may take place in mental effort. Unfortunately, we have very little definite and indisputable evidence on the relation of the height of blood pressure to efficiency. There is, however, what may be described as a certain amount of circumstantial evidence. We know, for example, that the rate of recovery from fatigue is dependent on the circulation. We may, therefore, consider it very possible that the increase in blood pressure and the consequent greater blood flow through the active part will reduce the liability to fatigue.

Considerable evidence to this effect has been collected by Cannon (11), who, with Nice, has demonstrated that there is great improvement in the contraction of a fatigued muscle on stimulation of the splanchnic nerve, an improvement which cannot be attributed to the secretion of adrenaline, since it occurs when the renal veins are tied. It is, however, well known that such stimulation would bring about a large rise in arterial pressure. If, as appears probable, there is a secretion of adrenaline in emotion, this hormone, as shown by Oliver and Schäfer (12) in their original paper, will improve muscular contraction. This has been confirmed by Cannon in relation to the intact animal but he found that this also occurred when minute doses of adrenaline, which bring about a fall in blood pressure, are used—a fact which suggests that in this instance the effect is due directly to the adrenaline rather than to the rise in blood pressure which occurs when large doses are injected. From the work of Gruber, in Cannon's laboratory, there seems little doubt, however, that the actual height of the blood pressure produced mechanically does have an appreciable effect on the power of a fatigued muscle to recover.

In this connection it is of interest to recall that the performance of immense feats of strength under conditions of exceptional stress is possible and may readily be associated with the high blood pressure which also presumably occurs in such circumstances.

In relation to the nervous system we

know that the reflexes disappear when the blood pressure becomes depressed below a certain critical level, and it may be agreed also that there is an increased cerebration in high blood pressure during lecturing. On the other hand it is very difficult to obtain any measurements of cerebration and it would be impossible to assert that persons with high blood pressure have a better cerebration than those whose blood pressure is low. This latter anomaly may, however, be due to the fact that there are many more causes of high blood pressure than psychic stimulation, *e.g.*, physical exercise.

It is, however, well recognized in games of skill needing muscular co-ordination, or in athletics, that periods of inefficiency or staleness may occur and that such periods may be produced by excessive repetition. No explanation has ever been given for this, but from the foregoing it seems not unlikely that some involuntary lack of interest or zest may be responsible, the more so as we have good reason to believe that such a lack of interest may reduce the contraction of the unrequired vessels (13). If this is so, there will not be the same rise in blood pressure, the same bracing up, for a given task that there is during periods of efficiency. Definite experimental evidence on this point is, however, lacking.

Of more general interest is the question why purely mental stress or interest should produce any bodily changes at all. It may be that these are accidental and of no value, possibly a physiologic relic of an age when a period of mental stress almost invariably preceded increased muscular activity; but from what has been said the possibility cannot be excluded that the rise in blood pressure which results, by shortening the warming up period, is of definite value in efficient muscular activity.

In conclusion it may be added that it is very evident that a more adequate understanding of the circulation may lead to the elucidation of some of the most important problems in industry and it is seen that intimate co-operation between physiology and hygiene is not only desirable but essential. We must believe that periods of inefficiency or ill health, which are observed by the hygienists, are definitely the result of some form of adverse environment. The function of the applied physiologist is to study how the environment may affect the body, to indicate in what direction further knowledge is required, and in due course to suggest remedial measures.

BIBLIOGRAPHY

1. McDowall, R. J. S.: The Physiology of Industrial Hygiene: I. The Relation of Industrial Fatigue to Gastric Ailments. This Jour., 1927, *9*, 427.
2. Hemingway, A., and McDowall, R. J. S.: The Chemical Regulation of Capillary Tone. Jour. Physiol., 1926–1927, *62*, 166.
3. Bayliss, W. M.: The Vasomotor System. Monographs on Physiology. London, Longmans, Green & Co., 1923.
4. Dale, H. H., and Evans, C. L.: Effects on the Circulation of Changes in the Carbon-Dioxide Content of the Blood. Jour. Physiol., 1922, *56*, 125.
5. Hill, L.: The Mechanism of the Circulation of the Blood. Schäfer's (E. A.) Text-Book of Physiology. Volume II. Edinburgh and London, Young

J. Pentland; New York, The Macmillan Co., 1900, p. 1.
6. Bainbridge, F. A.: The Physiology of Muscular Exercise. Monographs on Physiology. London, Longmans, Green & Co., 1923.
7. Mosso, A.: Fear. Translated from the Fifth Edition of the Italian by E. Lough and F. Kiesow. London, Longmans, Green & Co., 1896.
8. Gillespie, R. D.: The Relative Influence of Mental and Muscular Work on the Pulse-Rate and Blood-Pressure. Jour. Physiol., 1923–1924, *58*, 425.
9. Dawson: Discussion on Hyperpiesia. Brit. Med. Jour., 1925, *2*, 1161.
10. MacWilliam, J. A.: Some Applications of Physiology to Medicine. III.—Blood Pressure and Heart Action in Sleep and Dreams: Their Relation to Haemorrhages, Angina, and Sudden Death. *Ibid.*, 1923, *2*, 1196.
11. Cannon, W. B.: Bodily Changes in Pain, Hunger, Fear and Rage. New York, D. Appleton & Co., 1915.
12. Oliver, G., and Schäfer, E. A.: The Physiological Effects of Extracts of the Suprarenal Capsules. Jour. Physiol., 1895, *18*, 230.
13. McDowall, R. J. S., and Wells, H. M.: The Physiology of Monotony. Brit. Med. Jour., 1927, *1*, 414.

BOOK REVIEWS

Gewerbestaub und Lungentuberkulose (Stahl-, Porzellan-, Kohle-, Kalkstaub und Russ). Eine literarische und experimentelle Studie. By Dr. med. *K. W. Jötten*, o. ö. Professor der Hygiene und Direktor des Hygienischen Instituts der Westfäl. Wilhelms-Universität in Münster i. W.; and Dr. med. *W. Arnoldi*, ehemal. Assistent am Hygienischen Institut in Münster i. W. Paper. Pp. 256 with illustrations and bibliography. Schriften aus dem Gesamtgebiet der Gewerbehygiene, N. S. No. 16. Berlin: Julius Springer, 1927.

This excellent monograph opens with a thorough discussion of the literature on the subject and closes with an equally complete bibliography. These facts alone make it an indispensable part of any library on industrial hygiene.

In the introduction the authors make clear that the true relation of inhaled dust to tuberculosis is a matter of controversy. They believe light can be shed upon the subject through animal experimentation and probably better in this way than by statistical investigation of actual cases, the true condition of patients being so hard to ascertain.

The experiments utilized the following types of dust:

1. Steel grindings and filings: particles from 200 to 2 microns in diameter, many between 10 and 2 microns.

2. White porcelain dust: a silicate with the formula $4{\cdot}4\ Al_2O_3{\cdot}12{\cdot}6\ SiO_2$ plus contamination of different amounts of K_2O, Na_2O, CaO, MgO, and FeO. The SiO_2 content was 69.25 per cent. The average size of the particles was somewhat less than in the case of the steel dust, particles of 1.5 microns being plentiful.

A second variety of silicious dust contained more small particles but in other ways was not essentially different.

3. Coal dust: This contained many large particles but a sufficient number from 3 microns to 1 micron in diameter to be comparable.

4. Soot: again comparable in particle size.

5. Lime—chemically pure $Ca(OH)_2$: particle size comparable.

The animals employed were rabbits.

Control experiments established the fact that the strains of tubercle bacilli used could be relied upon to produce a widespread pulmonary tuberculosis when given by inhalation, the principal method of infection used by the investigators.

The dusts were given by means of inhalation apparatus of simple type and every effort was made to keep exposures uniform from day to day. One-hour dusting periods daily for several months were used to produce the pulmonary dust effects. Tubercle bacilli were given in a spray driven through dusting apparatus essentially similar to that used for the preceding dust inhalations.

The different dusts exercised an unfavorable influence—increased the severity of the tuberculous infection—in the following order: (1) steel dust; (2) both types of porcelain dust; (3) coal dust; (4) soot. Lime gave evidence of increasing the resistance to tuberculosis.

The monograph is thoroughly valuable for all interested in dust problems. Emphasis upon the danger of steel grindings has not been prominent in the United States, attention having centered upon the silicious dusts. The work of Jötten and Arnoldi, confirming previous experiments upon this point from the Leipzig laboratory, should be followed by clinical studies in this country.—*C. K. Drinker.*

CARL FLÜGGE'S GRUNDRISS DER HYGIENE, FÜR STUDIERENDE UND PRAKTISCHE ÄRZTE, MEDIZINAL- UND VERWALTUNGSBEAMTE. Tenth edition, revised by Dr. *Bruno Heymann*, A. O. Professor an der Universität Berlin. Cloth. Pp. 714 with appendix and index. Berlin: Julius Springer, 1927.

The revised edition of Flügge's well-known book on hygiene contains a chapter on industrial hygiene which deals practically entirely with conditions in Germany and includes none of the later work in this field in the United States or England. Since the book is designed for students who wish a thorough perception of the various fields of hygiene, it is unfortunate that this neglect of progress extends even to a failure to include references to work outside of Germany. The same deficiency is found in the chapters dealing with atmospheric conditions. —*C. K. Drinker.*

INTERNATIONAL CLINICS. Volume III. Thirty-Seventh Series, 1927. Cloth. Pp. 311 with index; illustrations. Philadelphia and London: J. B. Lippincott Co., 1927.

This volume contains twenty pages of exceedingly elementary material on the general subject of industrial hygiene.—*C. K. Drinker.*